The use of glycoprotein IIb/IIIa antagonists in acute coronary syndromes: are we following the NICE guidelines?

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Abstract

Recent developments in the management of non-ST elevation acute coronary syndromes (ACS) have included the introduction of glycoprotein (GP) IIb/IIIa inhibitors. The National Institute for Clinical Excellence (NICE) has published guidelines on their use, which state that these agents should be given to all high-risk patients.

Here, we present the results of a national survey of 1,000 consultant cardiologists and general physicians. A total of 361 replies were analysed: 98% of respondents treated patients with ACS and 92% of respondents had access to troponin assays. Overall, 241 (67%) of respondents prescribed GP IIb/IIIa inhibitors for ACS. There was a significant difference between cardiologists and generalists, with 194 (77%) cardiologists and 46 (42%) general physicians prescribing GP IIb/IIIa inhibitors in ACS (p=0.0013).

Despite the presence of government guidelines regarding the administration of GP IIb/IIIa antagonists in ACS, we calculate that only 32% of respondents are prescribing IIb/IIIa inhibitors as recommended by NICE.

Key words: glycoprotein IIb/IIIa antagonists, acute coronary syndromes, NICE guidelines.

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Introduction

In recent years, there have been major advances in the management of non-ST segment elevation acute coronary syndromes (ACS), including the introduction of glycoprotein (GP) IIb/IIIa antagonists.[1,2] The National Institute for Clinical Excellence (NICE) has published an appraisal on their use, which states that they should be given to all ACS patients who are considered to be at high risk of subsequent cardiac events or death.[3] Retrospective analyses of trials using GP IIb/IIIa inhibitors in ACS have shown that their benefits are greatest in patients with elevated troponin levels.[4-6] The initial recommendation from NICE, in 2000, was that serum troponin levels should be used to identify those patients who should receive GP IIb/IIIa antagonists.[3]

The aim of this study was to investigate current UK practice regarding use of cardiac markers and GP IIb/IIIa inhibitors in ACS.

Methods

A postal survey was sent to 600 consultant cardiologists and 400 randomly selected consultant physicians in general internal medicine (GIM) between February and March 2002. Replies were traceable to the hospital to which the survey was sent, but not to specific consultants.

Comparison between numbers of patients with ACS seen by cardiologists and by general physicians was made using the Mann-Whitney U test. Analysis of use of cardiac markers and GP IIb/IIIa inhibitors according to consultant type was carried out by chi-squared methodology.

Results

Response rates

The overall response rate was 38% (42% of cardiologists, 28% of general physicians). Nineteen replies were not useable, leaving a total of 361 replies for analysis. At least one reply was received from 183 of the 224 hospitals included in the study (82% of hospitals represented).

Sixty-three per cent of replies were from district general hospitals (DGH), compared with 17% from teaching hospitals and 19% from tertiary referral cardiology centres. Forty-four per cent of respondents described themselves as cardiologists, 26% as cardiologists plus GIM physicians and 31% as GIM physicians. GIM consultants saw significantly fewer ACS patients than cardiologists (median three patients per week for GIM and 10 patients for cardiology +GIM or cardiology, p<0.0001).

Forty per cent of DGH consultants who responded had a catheter laboratory (cath lab) at their hospital, although only

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Table 1. Frequency of use of cardiac markers

Cardiac marker	Frequency of use	Number	% (n=361)
CK	Frequent	274	76
	Rare	39	10
CK-MB	Frequent	69	19
	Rare	81	22
TnT	Frequent	188	52
	Rare	9	3
TnI	Frequent	138	38
	Rare	6	2
Other*		61	17

Key: *Myoglobin, ALT, AST, LDH; CK = creatine kinase; TnT = troponin T; TnI = troponin I; CK-MB = creatine kinase myocardial band isofraction

7% had any intervention performed on-site. This compared with 44% of teaching hospital consultants (24% intervention) and 100% of consultants from tertiary referral centres (100% intervention).

Availability and use of cardiac markers

The availability and use of cardiac markers are outlined in tables 1 and 2. Creatine kinase (CK) remains the single most widely used marker of cardiac damage, with 76% of respondents using it frequently or routinely. However, 14% of respondents are no longer using it at all. Ninety-two per cent of respondents now have access to measurement of either troponin I or T levels. Of the 28 respondents who do not have access to troponins, 16 use creatine kinase myocardial band isofraction (CK-MB), leaving 12 respondents stating that they have no access to specific markers of cardiac damage. When these replies were cross-checked with others from the same hospitals, only one hospital could be identified that genuinely had no access to troponin I or T, or to CK-MB. There was no difference in use of markers by cardiologists or GIM consultants.

Use of GP IIb/IIIa antagonists in ACS

Overall, 241 (67%) of respondents prescribed GP IIb/IIIa inhibitors for ACS. There was a significant difference between cardiologists and generalists, with 194 (77%) cardiologists and 46 (42%) general physicians prescribing GP IIb/IIIa inhibitors in ACS (p=0.0013). The indications for which these agents are used are described in table 3.

Of the 120 consultants who did not prescribe GP IIb/IIIa inhibitors, six (5%) treated no ACS patients and nine (8%) stated that they would send the patients to a cardiologist. However, overall, the group who did not prescribe GP IIb/IIIa inhibitors treated a median of five ACS patients a week, and 49% were cardiologists or had an interest in cardiology. The presence of a cath lab on-site increased the likelihood of a consultant prescribing a GP IIb/IIIa antagonist from 59% to 76%, although this was not significant (p=0.1434).

Discussion

This is the first survey of national use of GP IIb/IIIa inhibitors in ACS to be published that includes both cardiologists and general physicians, who are frequently involved in the initial care of these patients. Despite the presence of government guidelines regarding the administration of GP IIb/IIIa antagonists in ACS, we calculate that only 32% of respondents are prescribing them as recommended by NICE (i.e. to all high-risk ACS patients; the second group in table 3). Limiting the analysis to cardiologists or those with an interest in cardiology, 45% of respondents prescribe them according to NICE guidelines.

Thirty-three per cent of consultants reserved GP IIb/IIIa antagonists for patients likely to undergo angiography (thereby withholding treatment from most patients in whom intervention was not deemed appropriate for other reasons). Retrospective analyses of GP IIb/IIIa studies have shown that the greatest benefit is seen in those patients who proceed to intervention.[1,7] A recent meta-analysis has also suggested a small benefit in patients treated with GP IIb/IIIa antagonists, but not undergoing intervention.[5]

Ninety-two per cent of consultants had access to troponin measurements. Several respondents commented, however, that availability was restricted or that they had to send samples away for analysis, making them less useful for guiding acute management. A reworking of the NICE guidelines for prescribing GP IIb/IIIa blockers has recently been published.[8] This suggests a move away from using troponins as the sole indicator of high risk. It continues to recommend GP IIb/IIIa treatment for all patients with ACS who are at high risk, regardless of whether they are to undergo intervention.

Table 2. Application of cardiac markers

Marker	No. of respondents using marker frequently/routinely	To define MI*	To estimate size of MI*	Risk stratification*	To detect early reinfarcts*	For early discharge*
CK	274	86	49	8	30	9
CK-MB	69	77	36	13	32	19
Tn (T or I)	326	67	16	80	11	79

Key: *Per cent of number of respondents using marker frequently/routinely; CK = creatine kinase; CK-MB = creatine kinase myocardial band isofraction; TnT = troponin T; TnI = troponin I; MI = myocardial infarction

Table 3. Use of glycoprotein IIb/IIIa inhibitors in ACS

Indication for GP IIb/IIIa antagonist	Number of respondents	% of those who prescribe GP IIb/IIIa (n=241)	% of overall respondents (n=361)
Most patients with non-ST elevation ACS	7	3	2
All patients with non-ST elevation ACS stratified as high risk	114	47	32
ACS only if intervention planned or likely	80	33	22
Only for PCI after angiogram performed	32	13	9
Other	7	3	2

Key: ACS = acute coronary syndromes; PCI = percutaneous coronary intervention; NICE = National Institute for Clinical Excellence

The main issues limiting the prescribing of GP IIb/IIIa inhibitors in ACS are, however, financial. Many cardiologists remain unconvinced of the strength of data in favour of their use in those patients not undergoing revascularisation. It is therefore not surprising that many consultants choose to limit their prescribing of these agents to those patients likely to undergo intervention, in whom the greatest benefit might be achieved.

There were limitations to the study. The response rate was less than we had hoped for, particularly among the non-cardiologists, which may introduce bias. Importantly, however, at least one reply was received from 82% of the hospitals to which questionnaires were sent. There was a variation in responses from individual consultants in the same hospital (for example, there would be disagreement between consultants on availability of individual cardiac markers). Despite these limitations, the survey provides evidence that a significant number of consultants treating ACS are not prescribing GP IIb/IIIa inhibitors, and many of those who do prescribe them are not following current NICE guidelines for their use.

Key messages

- In a postal survey of UK consultant cardiologists and general physicians, only 67% of respondents prescribed GP IIb/IIIa inhibitors in acute coronary syndromes
- Prescribing was significantly higher among cardiologists than general physicians (77% *vs.* 42%, p=0.0013), despite almost all general physicians who responded regularly seeing ACS patients.
- Only 32% of respondents prescribed according to the NICE guidelines, i.e. to all high-risk ACS patients
- Many respondents reserved GP IIb/IIIa inhibitors for patients likely to undergo intervention

References

1. The Platelet Receptor Inhibition in Ischemic Syndrome Management in Patients Limited by Unstable Signs and symptoms (PRISM-PLUS) study investigators. Inhibition of the platelet glycoprotein IIb/IIIa receptor with tirofiban in unstable angina and non-Q wave myocardial infarction. *N Engl J Med* 1998;**338**:1488-97.
2. The PURSUIT Trial investigators. Inhibition of platelet glycoprotein IIb/IIIa with eptifibatide in patients with acute coronary syndromes. *N Engl J Med* 1998;**339**:436-43.
3. National Institute for Clinical Excellence. Technology appraisal guidance 12. Guidance on the use of glycoprotein IIb/IIIa inhibitors in the treatment of acute coronary syndromes. September 2000.
4. Cannon CP, Weintraub MS, Demopoulos LA *et al*. Comparison of early invasive and conservative strategies in patients with unstable coronary syndromes treated with the glycoprotein IIb/IIIa inhibitor tirofiban. *N Engl J Med* 2001;**344**:1879-87.
5. Boersma E, Harrington RA, Moliterno DJ *et al*. Platelet glycoprotein IIb/IIIa inhibitors in acute coronary syndromes: a meta-analysis of all major randomised clinical trials. *Lancet* 2002;**359**:189-98.
6. Heeschen C, Hamm CW, Goldman B, Deu A, Langenbrink L, White HD. Troponin concentrations for stratification of patients with acute coronary syndromes in relation to therapeutic efficacy of tirofiban. *Lancet* 1999; **354**:1757-62.
7. Chang W-C, Harrington RA, Simoons ML *et al*. Does eptifibatide confer a greater benefit to patients with unstable angina than with non-ST segment elevation myocardial infarction? Insights from the PURSUIT trial. *Eur Heart J* 2002;**23**:1102-11.
8. National Institute for Clinical Excellence. Technology appraisal guidance 47. Guidance on the use of glycoprotein IIb/IIIa inhibitors in the treatment of acute coronary syndromes. September 2002.